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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/344,189	06/24/1999	CHARLES E. ROGLER	0342/1D888US	8764

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EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
1632	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/344,189	Applicant(s) ROGLER ET AL.	
	Examiner Peter Paras	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment received on May 30, 2002 has been entered. Claims 1, 8, 15, 25, and 37-38 have been amended. New claims 39-41 have been added. Claims 1-41 are pending and are current under examination.

Claim Rejections - 35 USC § 112, 1st paragraph, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claims 1-38 under 35 U.S.C. §112, first paragraph has been withdrawn in view of Applicants amendments to the claims.

The following are new ground of rejection under 35 U.S.C. §112, first paragraph necessitated by Applicant's amendments to the claims:

New Matter

Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Independent claims 1, 8, 15, 25, 37-38 and 39 as amended now embrace an **immunetolerant mouse, which has a degenerated liver due to the presence of a secreted urokinase-type plasminogen activator (uPA)**.

The specification provides no implicit or explicit support for the context of the breadth of an immunetolerant mouse having a degenerated liver due to the presence of a secreted urokinase-type plasminogen activator (uPA) encompassed by the bolded clauses above. The section of the specification, page 5 lines 31-23, which Applicants have pointed to for support of such, in the Remarks section of the amendment, only supports immune tolerant mice with a degenerated liver that are hemizygous or homozygous for the urokinase-type plasminogen activator transgene.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP

2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

This rejection may be overcome with the following claim language (or similar acceptable language): an immunetolerant, transgenic mouse, which lacks functional T and B cells, whose genome comprises a urokinase-type plasminogen activator (uPA) gene, wherein expression of urokinase-type plasminogen activator results in liver degeneration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily

published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-5, 8-12, 15-21, 25-33, and 36-41 as originally filed, amended, or newly added are rejected under 35 U.S.C. 102(e) as being anticipated by Kay et al. The previous rejection is maintained for the reasons of record advanced on pages 6-8 of the Office action mailed on 11/23/01.

Applicant's arguments filed May 23, 2002 have been fully considered but they are not persuasive. Applicants have asserted that the specification of the '886 patent is not enabling for an immunodeficient mouse comprising a uPA transgene and having a liver reconstituted with human hepatocytes. In support of their contentions Applicants have provided a Declaration, under 37 CFR 1.132, by co-inventor Rogler. See the amendment on pages 6-9.

In response, the Examiner maintains that the '886 patent anticipates the claimed invention. The declaration under 37 CFR 1.132 filed May 22, 2002 is insufficient to overcome the rejection of claims 1-5, 8-12, 15-21, 25-33 and 36-41 based upon anticipation by Kay et al (the '886 patent) as set forth in the last Office action because: the evidence of lack of enablement of the specification of the '886 patent is secondhand. In particular, the Rogler declaration refers to conversations with co-inventor Kay, in which Kay suggested that the instantly claimed mice could not have been made using the guidance provided by Kay's specification. Such evidence is insufficient as it is secondhand. Moreover, every patent is presumed valid (35 U.S.C. 282), and that presumption includes the presumption of operability (Metropolitan Eng.

Co. v. Coe, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935). Also see the MPEP 716.07. Further, since in a patent it is presumed that a process if used by one skilled in the art will produce the product or result described therein, such presumption is not overcome by a mere showing that it is possible to operate within the disclosure without obtaining the alleged product. In re Weber, 405 F.2d 1403, 160 USPQ 549 (CCPA 1969). It is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments and adaptations, within the skill of the competent worker. The failures of experimenters who have no interest in succeeding should not be accorded great weight. In re Michalek, 162 F.2d 229, 74 USPQ 107 (CCPA 1947); In re Reid, 179 F.2d 998, 84 USPQ 478 (CCPA 1950). Finally, Applicants are reminded that even if a patent teaches or suggests the claimed invention, an affidavit or declaration by patentee that he or she did not intend the disclosed invention to be used as claimed by applicant is immaterial. In re Pio, 217 F.2d 956, 104 USPQ 177 (CCPA 1954).

Accordingly, the rejection is maintained for the reasons of record and as discussed in the preceding paragraphs.

Note, the upon re-reading Kay et al, the Examiner has concluded that Kay et al actually teaches away from using a transgenic mouse comprising a uPA transgene. It would appear that Kay intends for mice to be administered an adenoviral vector comprising a uPA gene rather than creating a uPA transgenic mouse. However, Applicant's claims are not limited to uPA transgenic mice and would embrace mice that comprise an *in vivo* transferred uPA gene via a vector of any kind. Should applicants

choose to limit the claims to a uPA transgenic mouse then the rejection may be withdrawn. The following claim language is suggested: an immunetolerant, transgenic mouse, which lacks functional T and B cells, whose genome comprises a urokinase-type plasminogen activator (uPA) gene, wherein expression of urokinase-type plasminogen activator results in liver degeneration.

It should also be noted that some of the claims (for example independent claims 8 and 38) are directed to a chimeric mouse model system for hepatitis. The claims do not recite any of the attributes of a model system for hepatitis. It is suggested that the claims be amended to recite specific characteristics that make the claimed mouse a model system for hepatitis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-13, 15-22, 24-34, and 36-41 as amended, originally filed, or newly amended are rejected under 35 U.S.C. 103(a) as being unpatentable over Kay et al taken with Alt et al. The previous rejection is maintained for the reasons of record set forth on pages 9-11 of the Office action mailed on 11/23/01.

Claims 7, 14, 23, and 35 as amended or originally filed are rejected under 35 U.S.C. 103(a) as being unpatentable over Kay et al taken with Alt et al as applied to

claims 1-6, 8-13, 15-22, 24-34 and 36-41 above, and further in view of Roggendorf et al. The previous rejection is maintained for the reasons of record set forth on pages 11-15 of the Office action mailed on 11/23/01.

Applicants have addressed both rejections with the same arguments. Accordingly, the following comments apply to both rejections. Applicant's arguments filed May 23, 2002 have been fully considered but they are not persuasive. Applicants assert that Kay does not teach a secreted uPA and that Alt and Roggendorf do not teach or suggest uPA induced liver degeneration. Moreover Applicants appear to be relying on the Rogler declaration, which attempts to suggest that Kay is not enabling for the disclosed mouse. See pages 9-10 of the amendment.

In response, the Examiner maintains that there is sufficient motivation to combine the teachings of Kay, Alt, and Roggendorf to arrive at the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Kay has taught a mouse that has uPA induced liver degeneration, wherein human hepatocytes may be implanted in the liver of said mouse, and wherein the human hepatocytes may be infected with hepatitis viruses, and wherein the mouse can have a SCID phenotype. Alt has taught

that a RAG-2 knockout mouse has an improved SCID phenotype and Roggendorf has suggested that woodchuck hepatitis virus and the woodchuck may be the most suitable model for human hepatitis B virus infection. As such ample motivation has been provided for combining the teachings of Kay, Alt, and Roggendorf to arrive at the claimed invention.

With regard to the Rogler declaration please refer to the Examiner's comments to that end, under the 102 rejections.

Accordingly, the rejection is maintained for the reasons of record and as discussed in the preceding paragraphs.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Patsy Zimmerman whose telephone number is (703) 308-0009.

Peter Paras, Jr.

Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER